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ANTIMICROBIAL CHEMOPROPHYLAXIS

Of the vast amount of antibiotics and other antimicrobial agents now being produced, a very large part is employed to prevent infection rather than for the treatment of actual infections. There are clear indications for such prophylaxis, but they are few. Most attempts at prophylaxis are likely to be ineffective; furthermore, they may lead to sensitization of the patient and toxic reactions; and in some cases instead of preventing infections, they cause superinfections.

INDICATIONS FOR PROPHYLAXIS - The prophylactic administration of penicillin or sulfonamides is of established value in preventing streptococcal infection and the recurrence of rheumatic fever in patients who have had previous attacks (The Medical Letter, May 15, 1959). Administration of penicillin or other antibacterial drugs to such patients prior to, during and after surgery and before and after dental extractions is also recommended for the prevention of bacterial endocarditis.

To help prevent rheumatic fever, bacterial endocarditis, and glomerulonephritis, whether or not there is a history of rheumatic fever, treatment with penicillin or other agents should be started promptly when any acute streptococcal infection, including scarlet fever, is discovered, and it should be continued for at least ten days (for preferred agents and dosages see the Medical Letter article cited above). Although L. Weinstein (N. E. J. of Med., 253: 679, 1955) found that the incidence of bacterial infections following measles was significantly greater in patients who had been treated prophylactically than in untreated patients, Medical Letter consultants believe that the doses used may have been inadequate and that antibacterial prophylaxis may be useful in preventing bacterial complications of measles. There is no disagreement, however, with Dr. Weinstein's statement (Ann. Int. Med., 43: 287, 1955) that the prophylactic use of antimicrobial agents in mumps, chicken-pox, varicella, infectious mononucleosis and pertussis has no beneficial effects, and that such prophylaxis in respiratory poliomyelitis increases the risk of pneumonia and other bacterial infections.

OTHER INDICATIONS - Penicillin provides effective protection against gonorrhea when it is administered after exposure. Eye instillation of penicillin also protects the newborn against gonorrheal ophthalmia. Sulfonamides are of definite value in protecting persons exposed to bacillary dysentery and meningococcal infection. A number of reports attest to the prophylactic value of pre-operative

oral administration of such non-absorbed agents as neomycin, streptomycin and certain sulfonamides in the preparation of patients for gastrointestinal surgery.

There are no other clear-cut indications for antibiotic prophylaxis; on the contrary, a number of carefully controlled studies indicate that efforts at prophylaxis may be harmful. Antimicrobial agents are often used in an attempt to prevent bacterial infection following colds and other viral infections of the upper respiratory tract. There is no well-documented proof that bacterial complications of upper respiratory infections are diminished by such attempts at prophylaxis.

Patients with acute heart failure are particularly susceptible to the development of pneumonia. R. G. Petersdorf and R. K. Merchant (N. E. J. of Med., 260: 565, 1959) report that prophylactic use of antibiotics in such patients was ineffective in preventing this complication. Their findings do not support the view that antibiotics should be given routinely to patients with congestive heart failure.

SURGERY - Antibiotics are often administered before or after surgery to control postoperative infections. Three carefully controlled studies indicate the undesirability of this procedure. M. D. Tachdjian and E. L. Compere (J. Internat. Coll. Surg., 28: 797, 1957) report that in 3,000 "clean" major orthopedic operations, 5.9% of 1900 patients given antibiotics prophylactically became infected, as compared with 2.6% of 1100 untreated patients. R. Sanchez-Ubeda, et al. (N. E. J. of Med., 259: 1045, 1958) studied 511 surgical cases and concluded that the prevalence of infectious complications is not affected by the routine administration of penicillin and streptomycin pre-operatively. R. S. Myers (Surg. Gyn. & Obst., 108: 721, 1959) found that in 1536 consecutive cases, postoperative infections following herniorrhaphy were three times as frequent in patients receiving prophylactic treatment as in patients not receiving such treatment. (Dr. Myers also noted that penicillin, streptomycin and tetracycline were most often used for such prophylaxis despite the fact that a very high proportion of hospital staphylococcal strains are resistant to these antibiotics.)

Antibiotic prophylaxis is often used by obstetricians following labor in the hope of preventing post-partum infection. Where the patient has a prolonged and difficult labor, such administration may possibly serve a useful purpose, but present evidence does not justify the routine use of antibiotic prophylaxis following delivery. Urinary infection following catheterization is an all too frequent occurrence even with rigid aseptic techniques, especially in the presence of an indwelling catheter. A high incidence of such infections occurs despite the prophylactic use of sulfonamides and other antimicrobials. The best way to minimize this possibility is to avoid catheterization, especially of the indwelling type, whenever possible.

The many authorities consulted by The Medical Letter were in full agreement in opposing the prophylactic use of antimicrobial agents except in the few conditions in which such prophylaxis is clearly indicated. Possible injury to the patient from sensitization, toxic reactions or superinfection is only part of the problem. The financial burden resulting from the needless use of expensive drugs can also be serious. Furthermore, the whole community suffers when increased bacterial resistance to antibiotics results from their wasteful use.

POLARAMINE AND DISOMER

The only thing basically new about two recently introduced antihistamines - Polaramine (Schering) and Disomer (White) - is their names. Polaramine is the dextro salt of chlorpheniramine maleate (Chlor-Trimeton--Schering). Disomer is the dextro salt of brompheniramine maleate (Dimetane-Robins) which in turn is the bromide analogue of chlorpheniramine maleate. (Robins uses the generic term "parabromdylamine" instead of "brompheniramine.") By omission of the inactive levo-isomer present in the older drugs, two milligrams of either of the new products becomes equivalent to four milligrams of the older ones.

Disomer, the advertising for this product tells us, "sheds the molecular dross." It has not been shown that such "shedding" has any greater significance to the patient than would result from a reduction in the amount of excipient in each tablet by a few milligrams. As with so many drugs, when claims of greater efficacy or potency mean only that the patient takes fewer milligrams of active ingredient in each oral dose, then the significance of the greater potency evaporates. Thus far, it has not been shown by controlled clinical trials that either Polaramine or Disomer represents an improvement over the older product in therapeutic effect or in absence of side effects.

ALL ARE GOOD - On the other hand, both Polaramine and Disomer, like Chlor-Trimeton and Dimetane, are good antihistamines, with a relatively low incidence of side effects. A recent double-blind study by I. W. Schiller and F. C. Lowell (N. E. J. of Med., 261:478, 1959) showed equal therapeutic effectiveness with Chlor-Trimeton and Dimetane, but with less frequent side effects, particularly sedation, with Dimetane. Another double-blind study (W. R. MacLaren, J. Allergy, 30:235, 1959) showed no significant differences in either therapeutic or side effects between Chlor-Trimeton and Dimetane.

All of these products cost about 4¢ to 6¢ per regular tablet, and there is little to recommend any one over the others. All are available in prolonged-action and syrup forms; Chlor-Trimeton and Dimetane are also available in ampules. As with all antihistamines, some work better for some persons than for others, and produce unwanted side effects in some persons and not in others. If Chlor-Trimeton or Polaramine is ineffective or produces undesirable reactions in a patient, then Dimetane or Disomer or any one of a number of other antihistamines may be worth trying (and vice-versa).

DIHYDROSTREPTOMYCIN AND KANAMYCIN

The New England Journal of Medicine has editorially called for an end to the production and marketing of dihydrostreptomycin, especially in packaged combinations with penicillin, on the ground that this antibiotic has no unique therapeutic virtues to compensate for the risk of irreversible deafness involved in its use (N. E. J. Med., Sept. 24, 1959). The New England Journal suggests that the Food and Drug Administration and the manufacturers take appropriate action. Both streptomycin and dihydrostreptomycin have such a high incidence of ototoxicity (the former affecting mainly balance, the latter, hearing) that physicians

have a grave responsibility when they administer either drug. The use in acute infections of dihydrostreptomycin alone or of the popular "combination" preparations containing dihydrostreptomycin and penicillin involves a serious risk of irreversible deafness even when small quantities are administered for one or two days (see The Medical Letter, May 1, 1959). The vestibular damage caused by streptomycin is generally not as serious as the hearing damage caused by dihydrostreptomycin, since most patients (except for the aged) can learn to compensate for the effects of damage to the sense of balance. If streptomycin must be used for the treatment of acute infections, it should be administered by itself, in minimal doses, and with daily observation of the patient for signs of eighth-nerve injury.

In the treatment of tuberculosis, there is a difference of opinion among Medical Letter consultants on the comparative hazards and value of streptomycin and dihydrostreptomycin. Some clinicians are convinced that dihydrostreptomycin should be used in tuberculosis despite the known risk of hearing loss.

KANAMYCIN - Physicians should also be extremely cautious about administering another antibiotic - kanamycin (Kantrex-Bristol), despite its promotion as the first antibiotic to use in staphylococcal and other infections. Kanamycin, like dihydrostreptomycin, can cause irreversible hearing loss; it should be used only in severe infections by sensitive organisms, and only after other safer agents have proved ineffective. As the pre-publication issue of The Medical Letter (Dec. 1958) pointed out, the toxic effects of kanamycin are similar to those of neomycin. With both, the risk of toxic effects is greater in patients with impaired kidney-function and it increases in proportion to dose and duration of treatment.

Reports of deafness resulting from the injection of kanamycin are appearing frequently in the medical literature, and not all involve large total dosage of the drug. As little as five grams was responsible for deafness in one case in which renal function was impaired (R. F. Naunton and P. H. Ward, AMA Arch. Otolaryng., 69: 398, 1959). Because kanamycin (like neomycin, which is identical in spectrum of activity and toxicity) can be life-saving in some cases, there is all the more reason to reserve it for serious systemic infections caused by staphylococci resistant to other and safer antibiotics and for urinary infections in which the organism has been determined to be sensitive only to kanamycin.

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Sworn to and subscribed before me this 9th day of October, 1959, Max Kalichstein, Notary Public, State of New York

Arthur Kallet, Managing Director

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